REMARKS

Claims 61-63, 65, 66, 77, 79-81, 86, 91, 93-101, and 104-115 were pending in the application. Claims 96-100 were previously withdrawn. Claim 61 has been amended and new claim 116 added. Support for the amendments can be found, for example, at page 7, lines 3-5, page 10, line 1-6, page 11, lines 18-21, page 26, lines 12-13, and Examples 3, 12 and 13. Accordingly, upon entry of the foregoing amendment, claims 61-63, 65, 66, 77, 79-81, 86, 91, 93-101, and 104-116 will be pending in the application.

No new matter has been added.

Applicants reserve the right to pursue the subject matter of the claims as originally filed or previously pending in this application or in another related application. In view of the foregoing claim amendments and the arguments set forth below, Applicants respectfully submit that the claims are now in condition for allowance.

Examiner Interview

Applicants thank the Examiner and her supervisors, Examiners Robert Zeman and Gary Nickol, for the courtesy of an in-person interview on April 12, 2011 with Dr. Jimmy Mond and Applicants' attorney. During the interview the present amendments to claim 61 and new claim 116 were discussed, as well as the rejection of claims 61-63, 65-66, 79-81, 86-87, 91, 94, 101 and 114-115 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description.

With respect to claim 61, Applicants have amended the claim to recite that the composition is effective to "provide protection against" staphylococcal infection in neonates. As discussed during the interview, Applicants' invention is directed to passive immunization as a means to protect a subject from bacterial infection. Passive immunization is the transfer of active humoral immunity in the form of antibodies to a subject. The Examiners agreed that Applicants' specification demonstrates that the claimed monoclonal antibodies provide protection against infection. Accordingly, claim 61 has been amended per agreement.

As suggested by the Examiners, new claim 116 has been added directed to a composition of an anti-LTA monoclonal antibody or antigen-binding fragment which is produced by a process in which the antibody is selected based on the characteristics set forth in claim. These

characteristics are also set forth in claim 61, as amended. The Examiners indicated that they would favorably consider new claim 116.

Rejection of claims 61-63, 65-66, 79-81, 86-87, 91, 94, 101 and 114-115 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description

During the interview with the Examiners, Applicants also discussed the rejection of claims 61-63, 65-66, 79-81, 86-87, 91, 94, 101 and 114-115 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description.

With respect to claim 77 which recites the CDRs of the monoclonal antibody 96-110, the Examiners indicated that this rejection is improper. Applicants request reconsideration and withdrawal of this rejection as applied to claim 77.

As stated in the Interview Summary of April 25, 2011, it is the Examiners' position that "the functional limitations of the instant claims do not overcome the written description rejection because Applicants have not identified the specific structural characteristics of the antibody that will correlate to the functional limitations in the instant claims."

Applicants respectfully disagree. To comply with the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventors had possession of the claimed invention.[1] Because the present claims are directed to monoclonal antibodies that bind a fully characterized antigen, poly-glycerol phosphate of LTA of *Staphylococcus*, and the production of monoclonal antibodies was routine at the time of Applicants' invention in 1997, the written description requirement has been met.

As amended claim 61 (and claims which depend there from) and new claim 116 are directed to a composition of a monoclonal antibody having the following characteristics:

(i) specifically binds to poly-glycerol phosphate of Lipoteichoic acid (LTA) of Staphylococcus, a well characterized antigen;

(ii) is of the IgG isotype;

[1] *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

(iii) binds to and enhances opsonization of multiple serotypes of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans* by phagocytic cells with or without complement as compared to an appropriate control in an *in vitro* opsonization assay; and

(iv) binds the same epitope to which MAB 96-110 antibody binds (the MAB 96-110 antibody produced by the hybridoma deposited at ATCC Accession No HB-12368).

Thus, the presently pending claims recite a set of structural and functional features common to all members of the genus, including the structural requirements that the monoclonal antibody specifically binds a fully characterized antigen, poly-glycerol phosphate of LTA of *Staphylococcus,* is of the IgG isotype, and binds the same epitope to which MAB 96-110 antibody binds.

Unlike a protein antigen, the poly-glycerol phosphate of LTA as a polymeric structure has the characteristics of a hapten, a simple antigenic determinant. Because haptens are single determinants as compared to most antigens which are comprised of multiple determinants the antibodies that haptens induce are very restricted and homogeneous in nature. One of the most well studied hapten is of a carbohydrate antigen. While the size of a carbohydrate antigen may be quite large, it is made of multiple repeating units of a single oligosaccharide unit, usually 1-5 sugars in length. Researchers have found that the antibody response to these haptens is determined by the oligosaccharide unit rather than by its conformation.[2] Because LTA is a linear polymer of repeating units of poly-glycerol phosphate it represents a simple antigenic determinant of known structure.

In addition, Applicants' specification teaches that a correlation between the structure of a monoclonal antibody which specifically binds poly-glycerol phosphate of LTA and the function of binding to and enhancing opsonization of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans* (*see e.g.,* Examples 2, 3 and 7). In particular, Example 1 of the present specification describes the preparation of monoclonal antibodies (and hybridomas) made using an antigen preparation from heat killed *S. epidermidis*. Examples 2 and 3 further show that the resultant antibodies are opsonic, and that they confer *in*

[2] V.L. Hegde and Y.P. Venkatesh *Immunobiology* 212 (2007) 119-128 (submitted as document C8 on the 1449 filed on July 17, 2009).

vivo protective effects against *staphylococci*. Example 7 of the specification further shows binding of an antibody within the scope of the present claims (Ab 96-110, also referred to as "A110") to LTA from *S. mutans*, *S. aureus* and *S. faecalis* (Tables 8 and 9 of the specification) and that it enhances the opsonization for both coagulase positive and coagulase negative staphylococci (see page 53, paragraph 2 of the specification). A chimeric version of this antibody was also created and shown to be opsonic and provide protective efficacy *in vivo* (see Examples 11-13 of the specification).

This disclosure provides a person of ordinary skill in the art with structural information for every member of the genus that falls within the scope of the claim as well as a correlation with the functional characteristics possessed by members of the genus and recited in the claims. In view of this disclosure, one skilled in the art would reasonably conclude that the inventors had possession of monoclonal antibodies which specifically bind LTA of *Staphylococcus* and enhance opsonization of multiple serotypes of *Staphylococcus epidermidis,* coagulase negative staphylococci, *Staphylococcus aureus* and *Streptococcus mutans*.

That Applicants provide a disclosure sufficient to demonstrate possession of the claimed genus of monoclonal antibodies is further demonstrated by the identification and characterization of additional anti-LTA antibodies within the scope of the present claims (*see, e.g.,* U.S. Pub. No. 2004/0052779). Two monoclonal antibodies, A120 and 391.4, having a high degree of sequence similarity to the A110 antibody (which corresponds to the same CDR regions as Ab 96-110 of the present application[3]), were identified by Applicants and shown to specifically bind LTA and bind to and enhance opsonization of Gram positive and negative bacteria.[4] In fact, the Applicants observed "the level of homology between the M110, M120, and MAb-391.4 variable regions may indicate that opsonic antibodies to LTA recognize a nearly identical epitope using nearly identical modes of binding, and that this mode of binding is important to their functional activity."[5]

Federal Circuit decisions, including *Centocor v. Abbott Labs*, and the USTPO Written Description Guidelines support Applicants' position. As stated by the Federal Circuit, the appropriate legal inquiry is whether "applicants has disclosed a 'fully characterized antigen,'

[3] Antibodies A110 and 96-110 differ only in the terminal amino acids of the light chain (*i.e.,* one amino acid difference on each of the N and C terminal positions).
[4] See Examples 1, 2, 5, 6, and 8 of the '779 Publication and Examples 2, 7, and 11 of the present Application.
[5] See paragraph [0196] of the '779 Publication.

either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen."[6] The court, when considering an antibody defined by function, has looked to the USPTO Written Description Guidelines as persuasive authority, stating that "a claim directed to 'any antibody which is capable of binding to antigen X' would have sufficient support in a written description that disclosed 'fully characterized antigens.'"[7] Example 14 of the revised Written Description Training Materials (Revision 1, March 23, 2008), clearly states that "an adequate description of a purified antigen would have put an inventor in possession of antibodies which bind to the purified antigen."

Recently, the Federal Circuit in *Centocor* confirmed that as long as the production of antibodies against a well-characterized antigen was "so routine that possessing the protein places the applicant in possession of an antibody." [8] Although the Court cautioned that a claim may not meet the written description requirement even if the protein is known, because antibodies with the claimed properties may not have been adequately described. In finding against Centocor, the Court stated

> Centocor simply failed to support its contention that ***generating fully-human antibodies*** with the claimed properties would be straightforward for a person of ordinary skill in the art ***given the state of human antibody technology 1994***. Unlike the antibody example in the PTO guideline, therefore simple possession of the known TNF-α protein did not place Centocor in possession of the claimed antibodies.[9] (emphasis added).

Centocor asserted claims to fully human antibodies without having described any in their specification, and the state of the art in 1994 was such that a human antibody could not be made using no more than routine techniques. Unlike *Centocor* the production of monoclonal antibodies was routine at the time of Applicants invention in 1997 and Applicant's specification describes the claimed invention in sufficient detail that one of ordinary skill in the art can reasonably conclude that the inventors were in possession of the claimed invention. Applicants, therefore, request reconsideration and withdrawal of this rejection.

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[6] *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004).
[7] *Id.*
[8] *Centocor Ortho Bio v. Abbott Labs* 636 F.3d 1341, 1352 (Fed. Cir. 2011).
[9] *Id.*

Conclusion

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance. If a telephone conversation with Applicants' attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 202-4626.

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Respectfully submitted,

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